Emergency Response and Medical Countermeasures for Radiological Incidents

Albert L. Wiley, BNE, MD, PhD, USNR(RET)

Director ,REAC/TS and WHO Collaborating Ctr.
Oak Ridge

ORAU National Security/ Emergency Management

NCI Radiation Epidemiology/Dosimetry Course 5/2011

albert.wiley@orise.orau.gov

A Clinical Therapeutic Strategy for Improving Survival of Patients with The Acute Radiation Syndrome(ARS)

1)Provide Emergency Medical/Surgical Patient Stabilization

2)Provide All and Appropriate Medical Supportive Care to Prevent Sepsis and Electrolyte/Protein/Fluid Imbalance

3)Identify/ Assess Dose and Source Term Specific Radiotoxicities of the Target Organs at Risk (Bone Marrow,GI, etc.)

4)Provide Appropriate Cytokines and Stem Cell Transplants

Example of ARS Medical Management – Chernobyl Patients

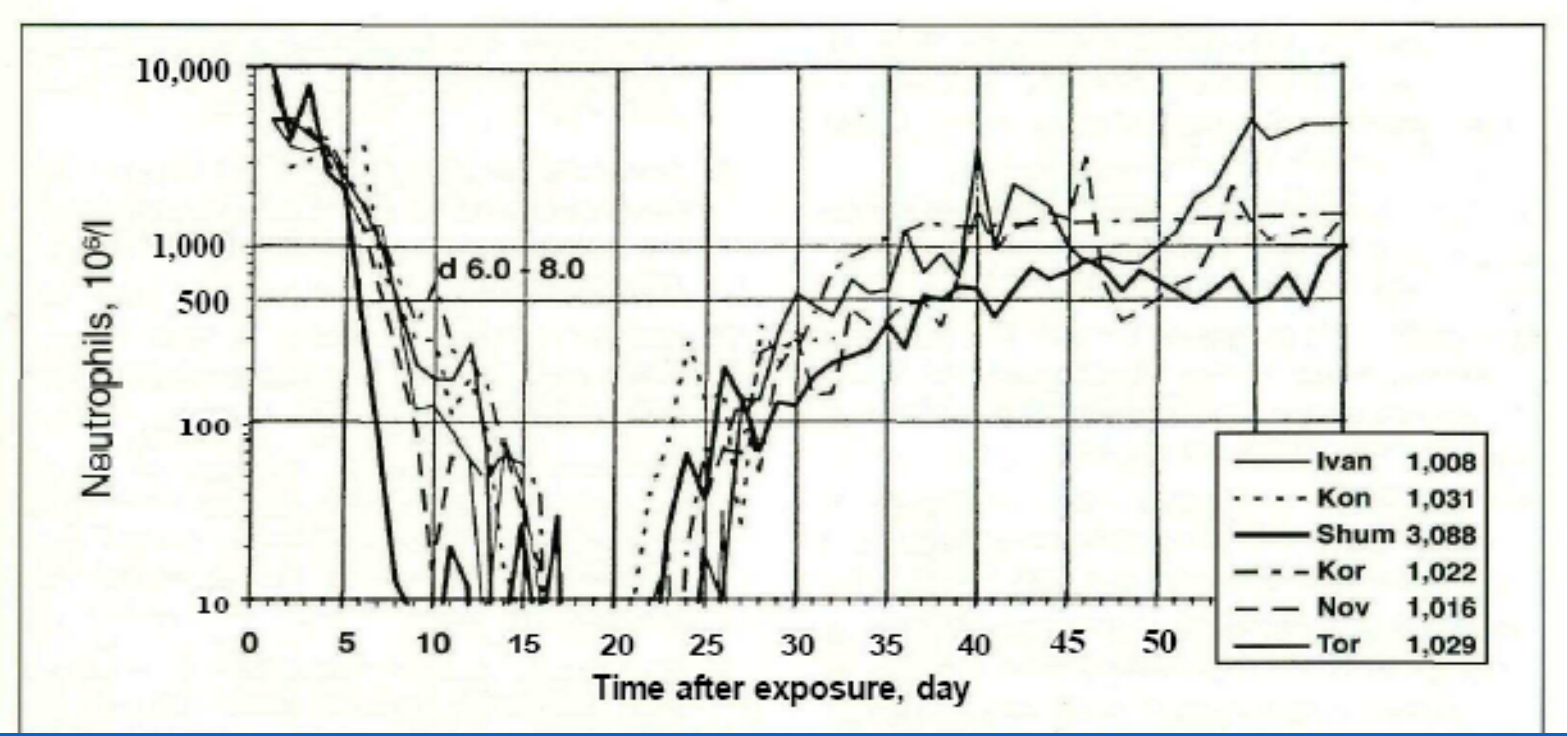
Critical cell counts and TIME post lethal TBI

1. ANC < 500/μL d8-14 (n=5)
   Estimated Dose 4.7-8.3 Gy
   All had ANC<100/μL; d12– 18

2. ANC < 500/μL d6-8 (n=6)
   Estimated Dose 7-9 Gy+
   All had ANC<100/μL; d8 –14

3. ANC <500uL d9-14; 6-8Gy (pre-Chernobyl)

Spontaneous Recovery of PMN Counts in 5 Liquidators Chernobyl, 4/26/1986



Shown are PMN counts for five individuals who had a PMN count of 500 per mm^3 6-8 days after exposure and who lived greater than 30 days. In no case was therapy with cytokines or stem cell transplanation administered.

Baranov A, et al., Stem Cells 13 (Suppl 1): 69-77, 1995.

Causes of Death in Chernobyl Victims

- Pnuemonia 4/13
  - Multiple Infections 2/13
  - Burns 4/13
- GI Damage 2/13

A. Baranov et al, New Engl J Med 321:205,1989

Infections in Tokai-Mura Cases

Patient	Role	Neutrons	Y-Rays	Transplant	Infections
A	Held Funnel	5.4Gy	8.5Gy	PB	• Candida albicans infection of anterior chest wall.
B	Poured fuel CB	2.9Gy (GVHD)	4.5Gy		• CMV infection treated successfully with Gangcyclovir • Methicillin-resistant *Staph aureus* unresponsive to Vanco and Aberkacin resulting in death from pneumonia on day 210.
C	Sat at desk	0.8Gy	1.3Gy	None	• Conjunctivitis (?) • Gingivitis 2° to IR

Supportive Care Components

- Fluids, blood products, nutrition

- administer based on clinical requirements/ symptoms

- Antibiotics?

- administered based on incidence of FN or neutrophil count (afebrile) after lethal exposure

IDSA, NCCN, clinical trials, Chernobyl

Treatment Components

Antibiotic prophylaxis should only be considered in:

- Afebrile patients who are expected to be profoundly neutropenia (ANC < 100/µL)
- Patients at the highest risk for infection

Medical Management

Cellular triggers for Medical Management

- ANC < 500/µL (afebrile) prophylactic
- ANC < 500/µL plus fever; febrile neutropenia
- Plt < 20,000/µL + Hct < 18

Clearly, serious hematopoetic depression from ARS must be averted to avoid lethal sepsis.

Thus, the limited clinical data base for an effective use of cytokines for ARS must be supplemented by animal data (basis for the FDA's "animal rule ").

Medical Management of the Acute Radiation Syndrome: Recommendations of the Strategic National Stockpile Radiation Working Group

Jamie K. Waselenko, MD; Thomas J. MacVittie, PhD; William F. Blakely, PhD; Nicki Pesik, MD; Albert L. Wiley, MD, PhD; William E. Dickerson, MD; Horace Tsu, MD; Dennis L. Confer, MD; C. Norman Coleman, MD; Thomas Seed, PhD; Patrick Lowry, MD; James O. Armitage, MD; and Nicholas Dainiak, MD

Physicians, hospitals, and other health care facilities will assume the responsibility for aiding individuals injured by a terrorist act involving radioactive material. Scenarios have been developed for such acts that include a range of exposures resulting in few to many casualties. This consensus document was developed by the Strategic National Stockpile Radiation Working Group to provide a framework for physicians in internal medicine and the medical subspecialties to evaluate and manage large-scale radiation injuries.

Individual radiation dose is assessed by determining the time to onset and severity of nausea and vomiting, decline in absolute lymphocyte count over several hours or days after exposure, and appearance of chromosome aberrations (including dicentrics and ring forms) in peripheral blood lymphocytes. Documentation of clinical signs and symptoms (affecting the hematopoietic, gastrointestinal, cerebrovascular, and cutaneous systems) over time is essential for triage of victims, selection of therapy, and assignment of prognosis.

Recommendations based on radiation dose and physiologic response are made for treatment of the hematopoietic syndrome. Therapy includes treatment with hematopoietic cytokines; blood transfusion; and, in selected cases, stem-cell transplantation. Additional medical management based on the evolution of clinical signs and symptoms includes the use of antimicrobial agents (quinolones, antiviral therapy, and antifungal agents), antiemetic agents, and analgesic agents. Because of the strong psychological impact of a possible radiation exposure, psychosocial support will be required for those exposed, regardless of the dose, as well as for family and friends. Treatment of pregnant women must account for risk to the fetus. For terrorist or accidental events involving exposure to radioiodines, prophylaxis against malignant disease of the thyroid is also recommended, particularly for children and adolescents.

Ann Intern Med. 2004;140:1037-1051. www.annals.org

For author affiliations, see end of text.

Recommended Doses of Cytokines

Cytokine	Adults	Pediatrics	Pregnancy*	Precautions
G-CSF or Filgrastim	5 ug/kg per day SC, and continued until ANC >1,000 cells/mm^3	5 ug/kg per day SC, and continued until ANC >1,000 cells/mm^3	Class C+ (same as adults)	Sickle cell hemoglobinopathies, significant coronary artery disease, ARDS. Consider discontinuation if pulmonary infiltrates develop at neutrophil recovery.
Pegylated G-CSF or Pegfilgrastim	6 mg, SC x 1 dose	For adolescent >45 kg: 6 mg, SC x 1 dose	Class C (same as adults)	Sickle cell hemoglobinopathies, significant coronary artery disease, ARDS.
GM-CSF or Sargramostim	250 ug/m^2 per day, SC, and continued until ANC >1,000 cells/mm^3	250 ug/m^2 per day, SC, and continued until ANC >1,000 cells/mm^3	Class C (same as adults)	Sickle cell hemoglobinopathies, significant coronary artery disease, ARDS. Consider discontinuation if pulmonary infiltrates develop at neutrophil recovery.

+Class C: Refers to US Federal Drug Administration Pregnancy Category C; studies have shown, teratogenic and/or embryocidal effects in animals but there are no controlled studies in women.

*Experts in biodosimetry must be consulted. Any pregnant patient with exposure to radiation should be evaluated by a health physicist and maternal-fetal specialist for an assessment of risk to the fetus.

Abbreviations: Absolute Neutrophil Count (ANC), Subcutaneous (SC), Acute Respiratory Distress Syndrome (ARDS).

Three Useful Sources of Hematopoietic Stem Cells

- **Bone Marrow**
- **Peripheral Blood Stem Cells (PBSC)**
- **Umbilical Cord Blood**

C.W. Bill Young Cell Transplantation Legislation

- US Congress Legislation, now signed into law.
- Builds on a 20 year history of Federal support for unrelated donor hematopoietic cell transplantation
- Signals clear governmental support of cord blood banking and transplantation
- Requires planning for radiation emergencies:
- * CW "Bill" Young, US Representative in Congress(10th Congressional Dist., Fla.)

CW Young Cell Transplant Legislation (continued)

- The adult donor and cord blood functions shall-
- "..maintain and expand medical contingency response capabilities,in coordination with Federal programs,to prepare for and respond to biological,chemical,or radiological attacks,and other public health emergencies that can damage marrow,so that the capability of supporting patients with marrow damage from disease can be used to support casualties with marrow damage;,,"

US Medical Response to a Nuclear Accident or Terrorist Event

There is currently in the US medical community consideration of a treatment protocol consisting of several components ,based on the US Strategic Stockpile Working Group Paper(Waselenko, et al.):

Key Elements:

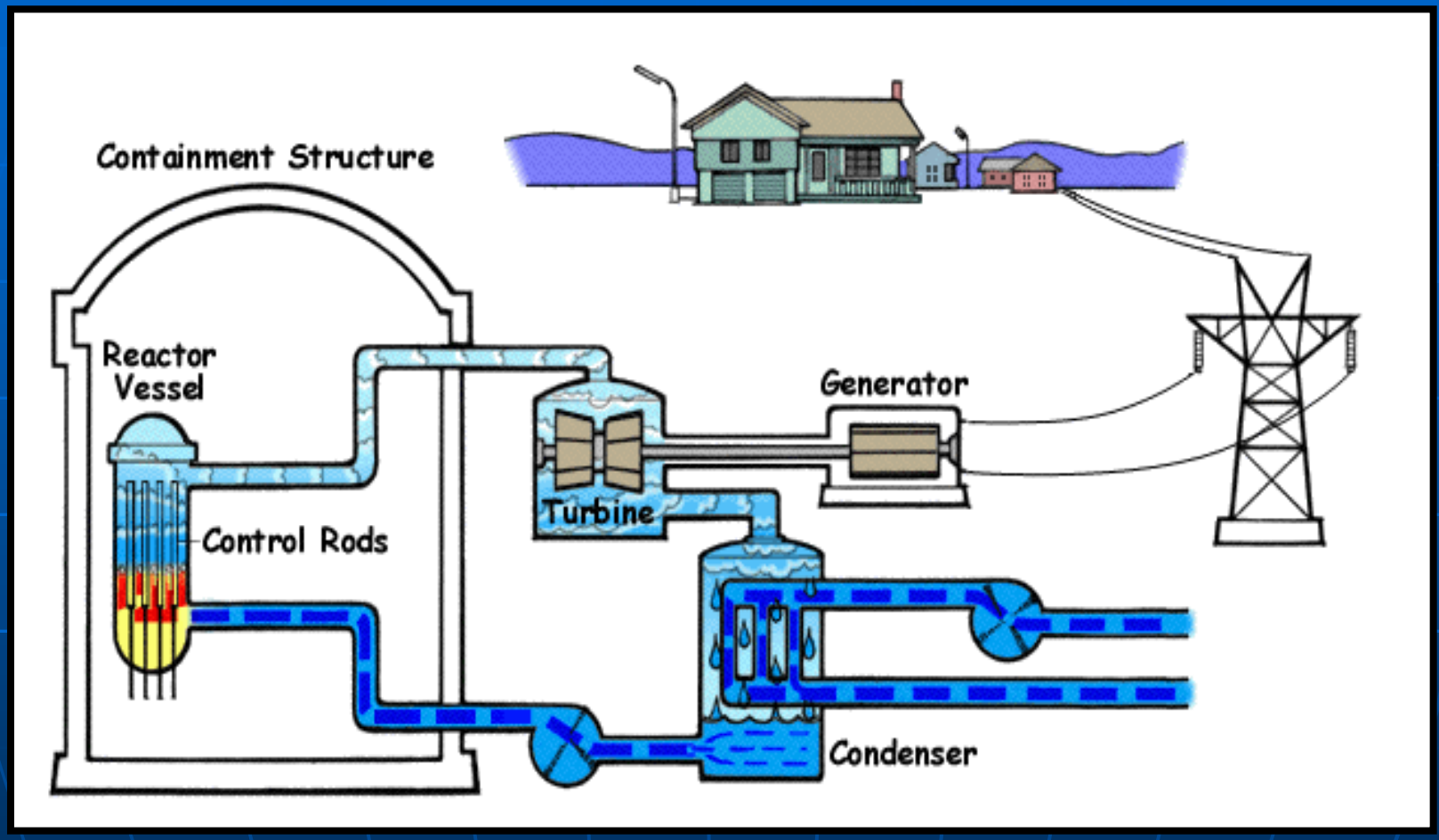
1.Supportive Care

2. Hematopoetic growth factors (cytokines) and stem cell transplants

Nuclear Power Plants as Source Terms for Internal Contamination

- Familiarize with the basic characteristics of nuclear power plant accidents
- Describe planning guidelines and considerations for accident response

Nuclear Reactor Schematics



Boiling Water Nuclear Reactor

Reactor Accidents

- Loss of Coolant Accident (LOCA)
- Pipe breaks in the primary loop remove cooling water from the core, leading to an increase in core temperature
- Fuel rods fail, releasing volatile radionuclides (iodine, cesium, etc.)
- Core meltdown—all the way to China?

What Really Happens

- Fuel expands, reducing reaction rate
- Reactor scrams with gravity-induced lowering of control rods
- Emergency core cooling system activates and floods core
- Even if core does melt, containment systems works, as at TMI

Reactor Accidents

- Most likely route of exposure to the public would be a release to the air.
- Plume materials could consist of particulates, vapors, mists, or gases.
- Plume could be short duration (puff) or continuous.
- Particulates will tend to settle to the ground as the plume drifts from the plant.

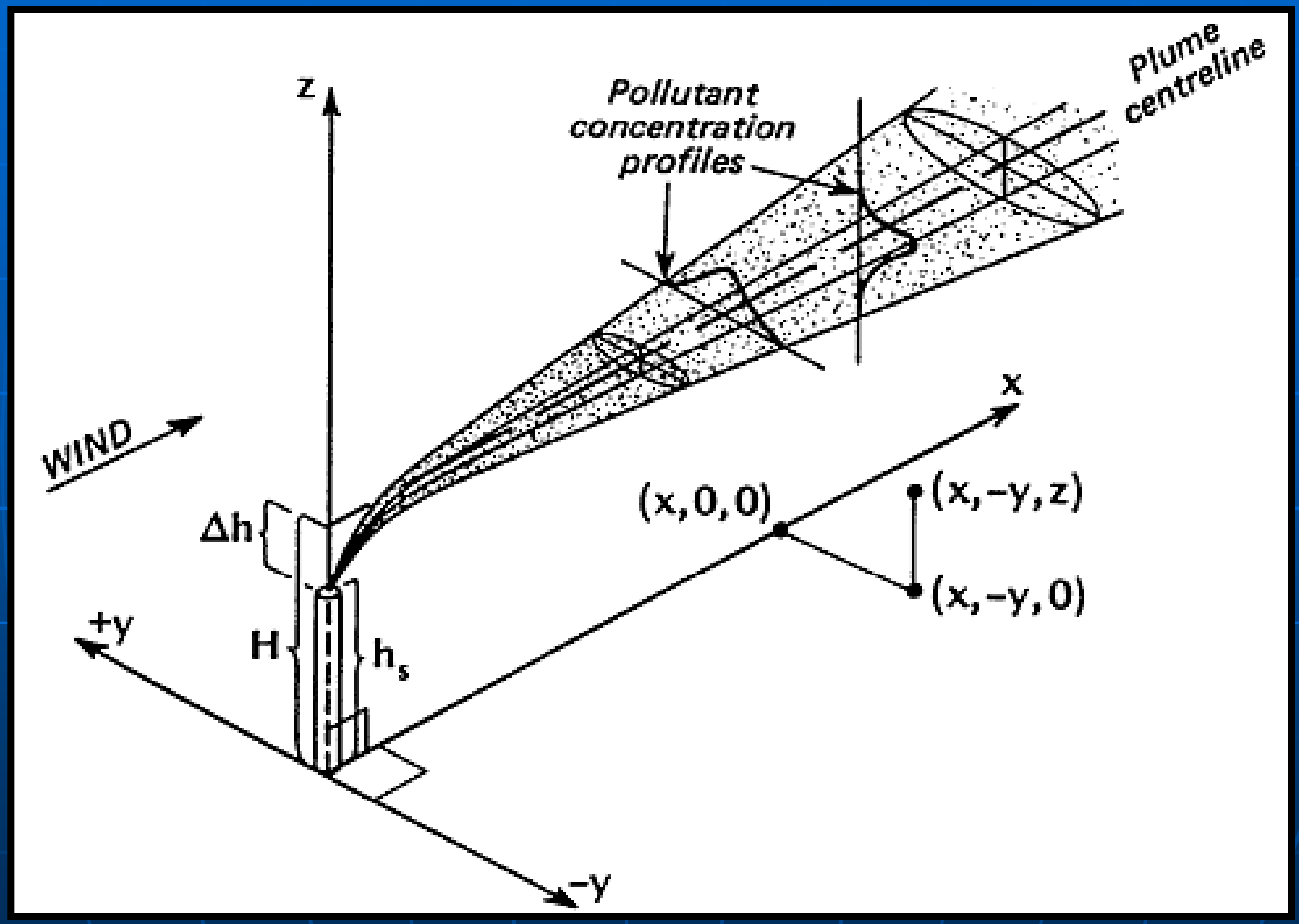
Atmospheric Releases

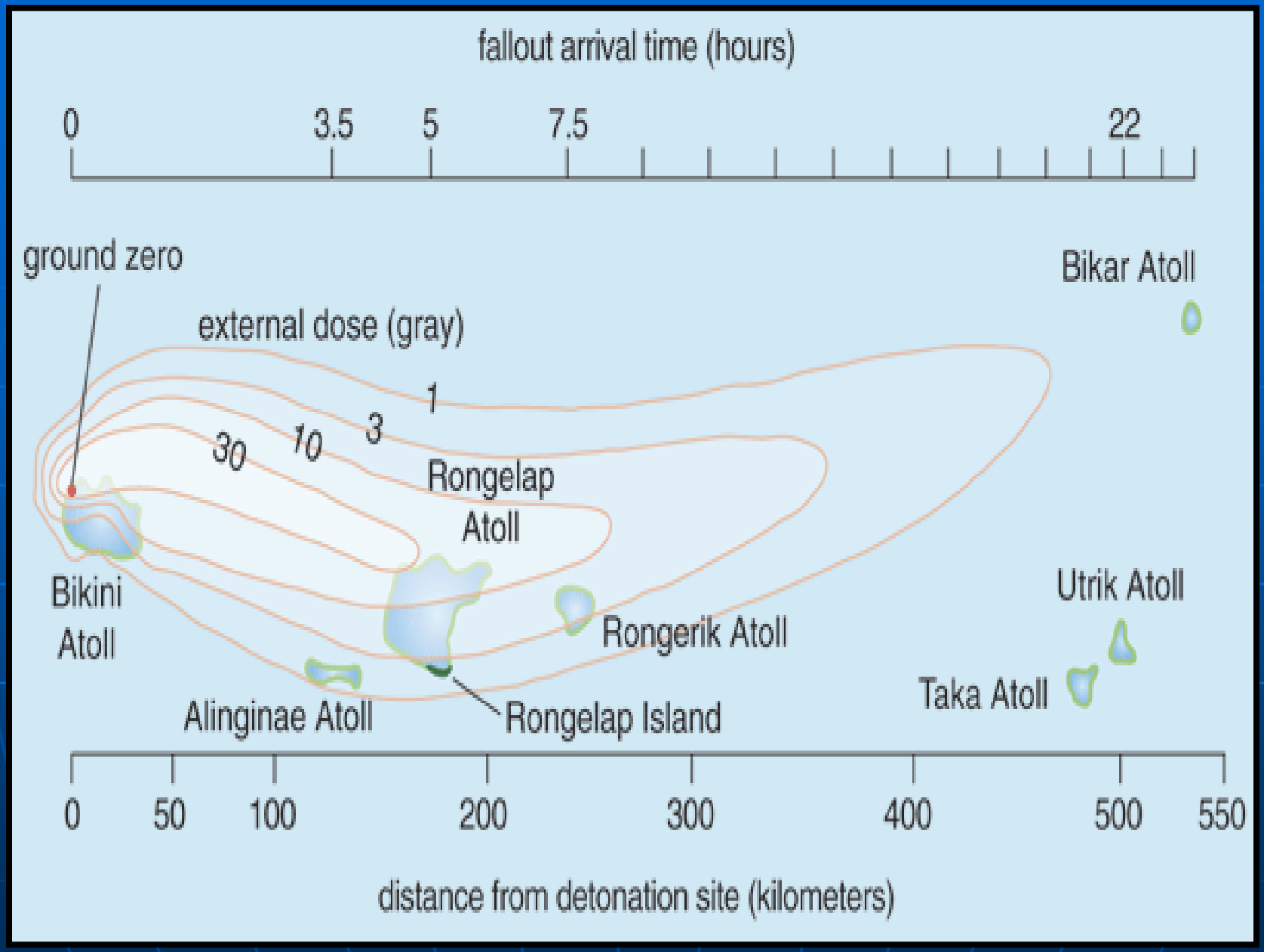
- Volatile radionuclides may be released from containment
- Principal radionuclide of concern is ^{131}I
- Releases are monitored by sensors placed around plant
- Plume dispersal is mathematically modeled, taking local terrain into account

Airborne Radioactivity

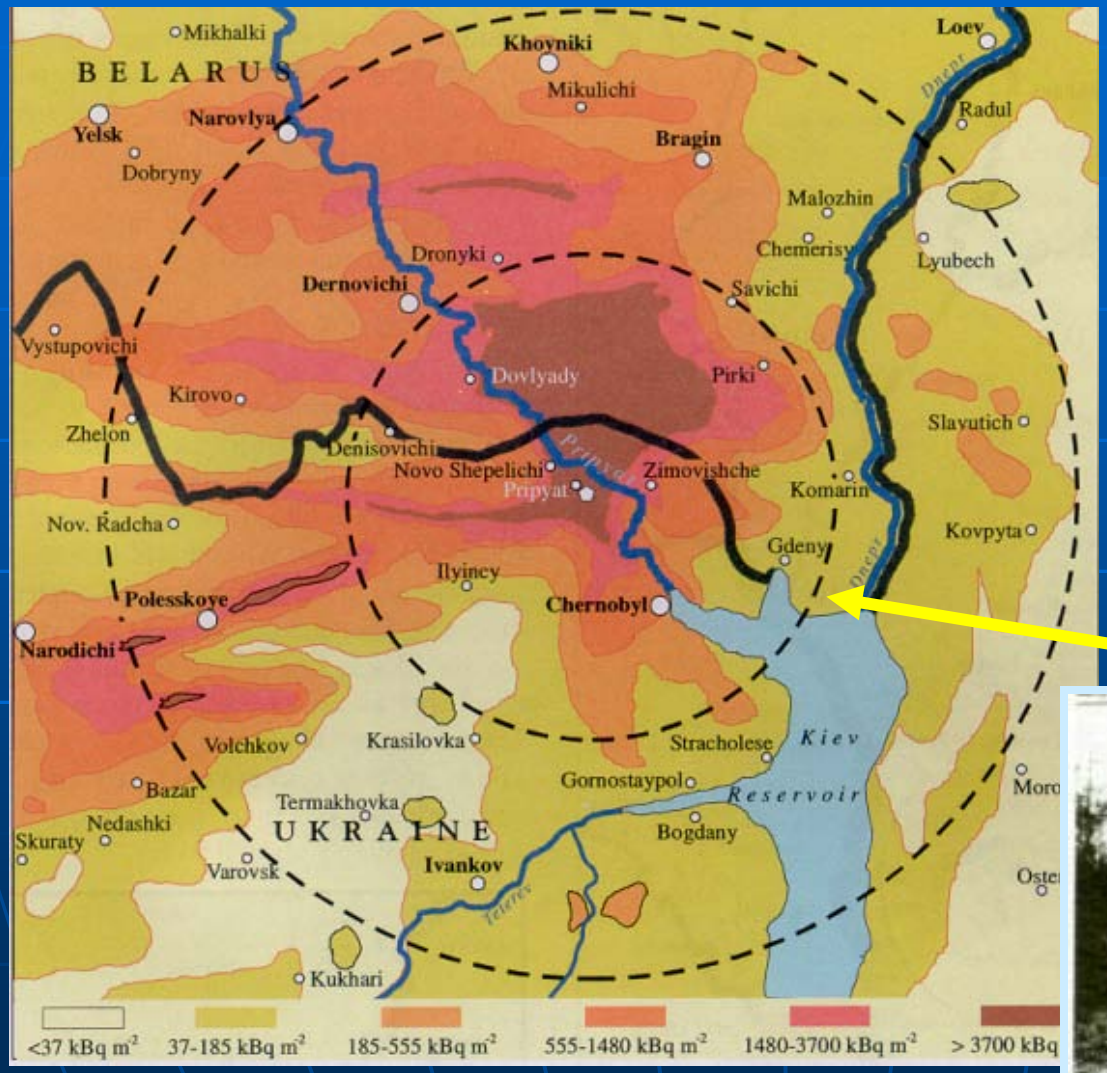
- **"Source term" - source of the exposure**
  - examples - stack effluent, burning aircraft, etc.
  - complex function of the material (quantity and type), flow rate,distribution,etc.
  - units - activity/unit of time (e.g., Ci/sec; Bq/sec)
- **Population/personnel exposure**
  - airborne (radioactivity) concentration [µCi/ml; Bq/m^3]
  - resuspended (ground/surface) contamination [$\mu Ci/ft^2$; $Bq/m^2 \rightarrow \mu Ci/ml$; Bq/m^3]

Plume Dispersion




fallout arrival time (hours)
0
3.5
5
7.5
22
ground zero
Bikar Atoll
external dose (gray)
1
3
10
30
Rongelap
Atoll
Bikini
Atoll
Utrik Atoll
Rongerik Atoll
Taka Atoll
Alinginae Atoll
Rongelap Island
0
50
100
200
300
400
500
550
distance from detonation site (kilometers)

Contamination Around Chernobyl NPP (1986)



Exposure Pathways

- External dose from plume overhead (cloud shine) or material on ground (ground shine).
- Internal dose due to inhaling materials directly from plume or from stirred dust.
- Ingestion of contaminated materials in the form of food or water.

Emergency Planning Zone

- Areas for which planning is needed to assure that prompt and effective actions can be taken to protect the public
- Plume EPZ: radius of approximately 10 miles
- Ingestion EPZ: radius of approximately 50 miles

Exclusion Area

- An area surrounding the plant such that an individual located at any point on its boundary will not receive a dose to the whole body exceeding 250 mSv (25 rem) nor a dose to the thyroid exceeding 3 Sv (300 rem) within 2 hours of the postulated incident

Classification of Emergencies

- Unusual Event: a potential degradation of the level of safety of the plant
- Alert: readiness of on-site and off-site response organizations increased.
- Site Area Emergency: event resulting in major decrease in protection of public or on-site personnel.
- General Emergency: event resulting in risk requiring implementation of urgent off-site actions.

Accident response

- Independent of the type of accident:
  - determine and control hazards to responders & victims
  - assess, treat, evacuate victims
  - implement further control procedures
  - assess personnel exposures
  - monitor clean-up
  - verify clean-up effectiveness

Exposure Guidance for Responders

- All activities:
  - 5 rem TEDE, 15 rem eye, 50 rem organ
- Protecting major/valuable property:
  - 10 rem TEDE, 30 rem eye, 100 rem organ
- Life saving or protecting large populations:
  - 25 rem TEDE, 75 rem eye, 250 rem organ
- Exceed latter only on a voluntary basis by persons fully aware of risks involved

Additional Guidance for Responders

- Risk of injury in rescue and recovery operations shall be minimized
- Risks to responders shall be weighed against benefits to be gained
- Rescue actions involving substantial personal risk shall be performed by volunteers
- Each individual subjected to emergency dose limits shall be thoroughly briefed

Some More Guidance for Responders

- Volunteers above age of 45 preferred
- TEDE shall not exceed 1 Sv (100 rem)
- Internal exposure should be minimized
- Exposure under such conditions should be limited to once in a lifetime
- Persons receiving exposures above 250 mSv (25 rem) should avoid procreation for several months

Guidance for Population Protection: 1st Principle

- Intervention to avoid serious prompt health effects should be carried out as a first priority
  - serious prompt health effects may be expected in susceptible populations at doses > 1 Gy (100 rad), and in all at doses > 2 Gy (200 rad) (whole-body)
  - evacuation is usually the only effective intervention measure in high dose situations

Guidance for Population Protection: 2nd Principle

- Protective actions to avoid delayed health effects should be initiated when they will produce more good than harm in the affected population
  - iodine prophylaxis in case of radioiodine releases
  - sheltering in place, evacuation, or temporary relocation

Guidance for Population Protection: 3rd Principle

- These actions should be introduced and withdrawn at levels that produce a maximum net benefit to the population
  - guidelines available from USEPA, IAEA, and IRPA
  - may well be driven primarily by logistical considerations (e.g., availability of transport, availability of temporary shelters, etc.)

Protective Actions Available to the Public

- Sheltering
- Evacuation
- Stable Iodine Prophylaxis
- Other actions to reduce dose

Guidelines for Protective Actions

- Early phase: initiation of release to about 4 days
- Evacuate to avoid TEDE of 1 - 5 rem
- Shelter in place if equal or greater protection afforded by doing so
- Administer KI to prevent thyroid dose of 25 rem

Logistical Requirements for Early Protective Actions

- Sheltering:
  - Normal emergency services; additional police
- Evacuation:
  - Transportation
  - Temporary housing (schools, tentage, etc.)
  - Food and water
  - Sanitation
- Iodine prophylaxis:
  - KI tablets (or tincture of iodine on skin)

Intermediate Phase PAG's

- Intermediate phase: source or release is under control, and additional protective actions are being implemented; weeks to months
- Relocate to avoid 2 rem TEDE or 100 rem to skin in first year
- Apply dose reduction techniques (e.g., decontamination, hot spot removal) if less than 2 rem TEDE anticipated in 1st year

Late Phase PAG's

- Late phase: recovery phase; site remediation and long-term mitigation; months to years
- TEDE not to exceed 0.5 rem in any year after the first
- Cumulative dose (TEDE) from all years not to exceed 5 rem

Logistical Requirements for Later Protective Actions

- Temporary relocation:
  - Transportation
  - Housing & furnishings
  - Security
  - Decontamination equipment & waste disposal
- Permanent resettlement:
  - Transportation
  - Housing & furnishings
  - Security

Food Chain Considerations

- Early times: radioiodine pathway is air to soil to vegetation to cow to milk to man
- Late times: cesium and strontium pathways include
  - air to soil to food plants to man
  - air to soil to forage plants to food animals to man
  - air to water to aquatic vegetation to fish to man

Logistical Requirements for Control of Food and Water

- Monitoring capability
- Centralized distribution
- Alternate (distant) sources
- In case of food shortages, alternate (higher) action levels should be instituted

Summary

- Medical planning concerns for a nuclear incident may range from zero to numerous serious casualties
- Public health concerns grow exponentially with sheltering, evacuation, and contamination of food supplies
- Don’t forget the psychological aspects

Medical Countermeasures: Definition of Internal Contamination

The deposition of radioactive material inside the body.

Common Routes of Entry

- Inhalation
- Ingestion
- Absorption through wounds or skin
- Injection

Inhalation Pathway

- Size of the aerosol particles determine region of the respiratory tract where most are deposited.
- Fate of inhaled particles is dependent on their physico-chemical properties.
  - Highly insoluble particles remain in the lung for long periods of time.
  - A small fraction will be transported to the tracheo-bronchial lymph nodes by pulmonary macrophages.
  - Some are cleared through the airways, swallowed, and excreted in the feces.

Potential Exposure Situations

- Stages of the nuclear fuel cycle

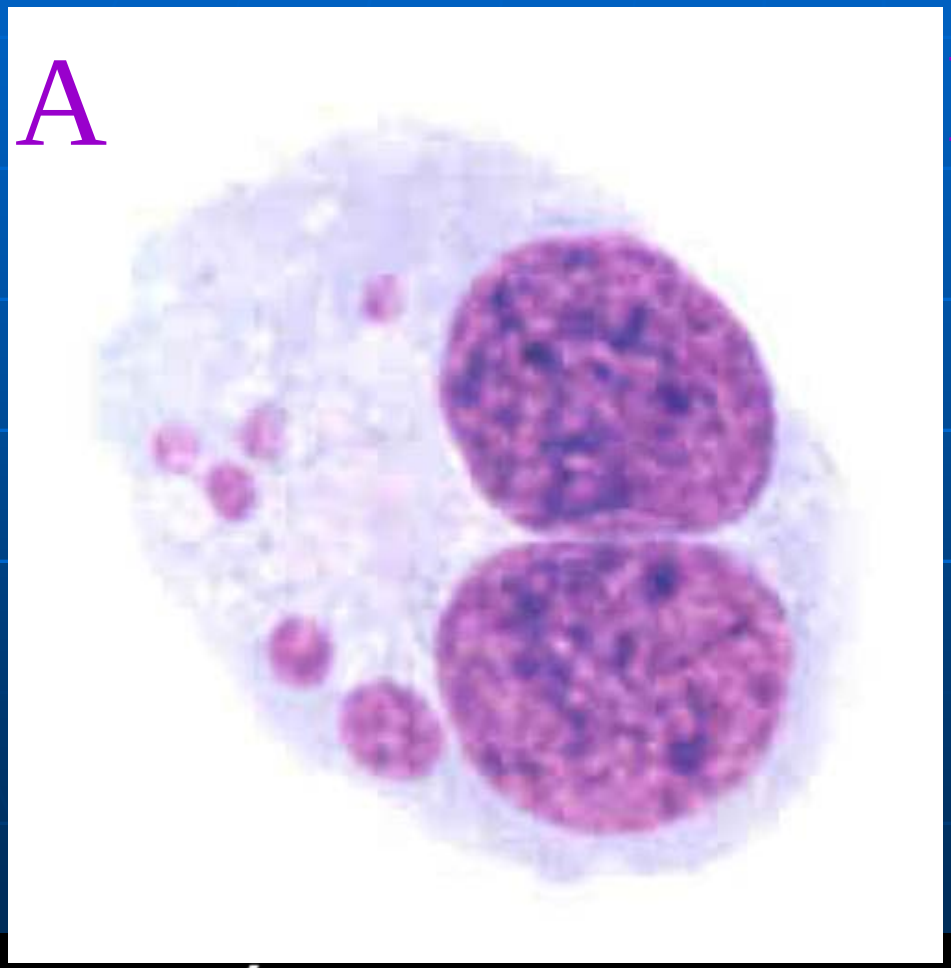
- Accidental intake with radioactive sources:
  - Medical.
  - Industrial.
  - Environmental uptake associated with accidental or intentional releases of radioactivity (e.g. reactor accidents, terrorist activity).

Methods for Assessing Intakes

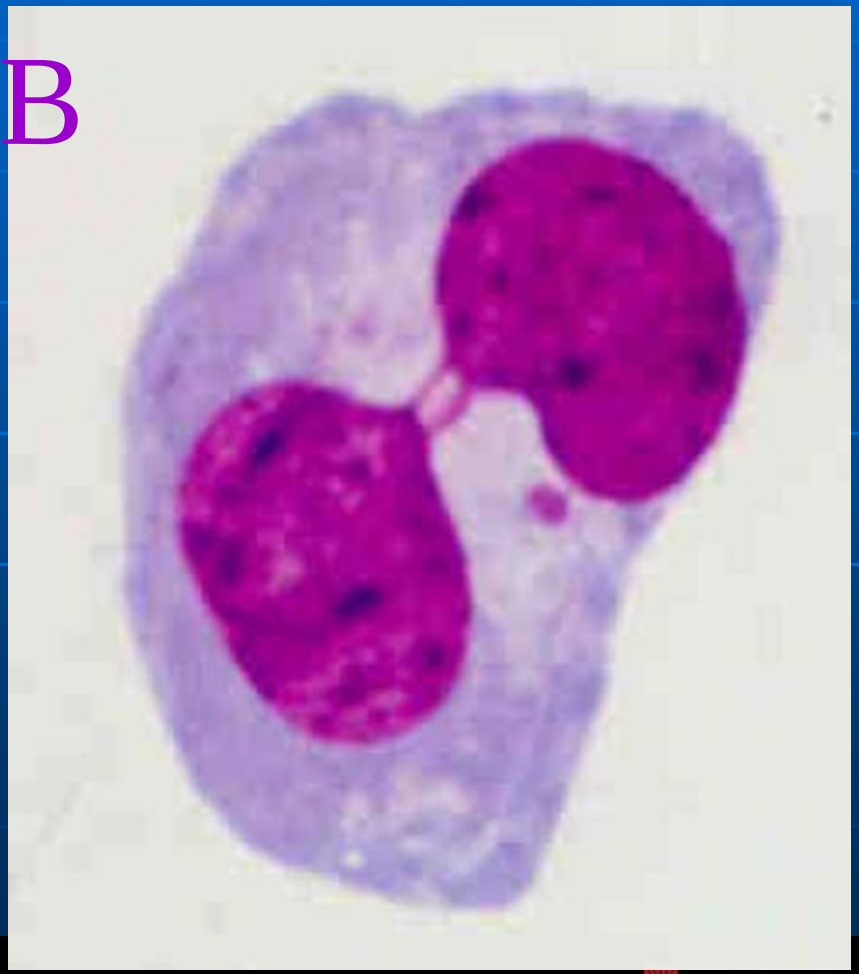
- Whole Body Counting:
  - Feasible for nuclides that emit penetrating x or gamma rays.
  - Useful also for nuclides emitting energetic beta particles - can be detected by their bremsstrahlung radiation.
- Bioassay:
  - Urine - most widely used.
  - Feces.
  - Excised material from wounds.

MN and nucleoplasmic bridges in binucleated cells (Giemsa stained)

A



B



When to Treat?

- ALI (annual limit of intake) is intake necessary to give a CEDE of 5 rem = 0.05 Sv.
- For intake < 1 ALI, no treatment.
- For 1< intake < 5 ALI, possible treatment, with physician discretion. For 5 < intake < 10 ALI, seriously consider treatment.
- For intake > 10 ALI, treat with patient consent.
- New NCRP 65 committee considering a unit, CDL (clinical decision limit) = 5 ALI.

Internal Contamination Treatment? (Guidelines for Industrial Accidents)

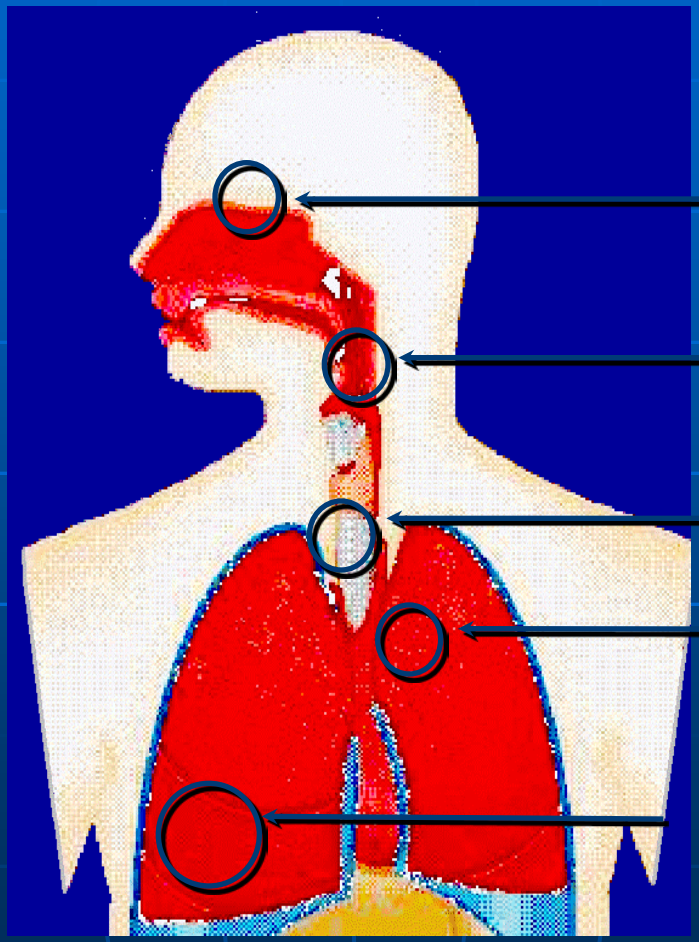
- ALI (annual limit of intake) is that CEDE necessary to give 5 rem = 0.05 Sv.
- For intake < 1 ALI, no treatment.
- For 1< intake < 5 ALI, possibly no treatment, with physician discretion.
- For 5 < intake < 10 ALI, consider treatment.
- For intake > 10 ALI, probably treat ,with patient consent.

Consenus needed for mass casualty plans!

Treatment Methods

- Minimize intake.
- Reduce and/or inhibit absorption.
- Block uptake.
- Use isotopic dilution.
- Promote excretion.
- Alter chemistry of the substance.
- Displace isotope from receptors.
- Chelate.

Particle Size Distribution in the Respiratory Tree



Particle Size (Micron, Mass Median Diameter)

18-20
15-18
7-12
4-6 (bronchioles)
1-5 (alveoli)

Clearance Time of Respiratory Tract

	Hours
Trachea	.1
Bronchi	1.0
Bronchioles	4.0
Terminal Bronchioles	10.0
Alveoli	100.0 Days+

Clearance Time of Gastrointestinal Tract

	Occupancy Time (Hours)
Stomach	6
Small Intestine	14
Upper Large Intestine	18
Lower Large Intestine	22

How to Reduce of Absorption From Gastrointestinal Tract

- Antacid
- Precipitation into insoluble salt
- Catharsis
- Ion exchange

Tritium - ^{3}H

- Follows pathway of water in the body.
- Penetrates skin, lungs, and GI tract, either as tritiated water (HTO) or in the gaseous form.
- Single exposures are treated by forcing fluids.
- This has the dual value of diluting the tritium and increasing excretion.
- Biological half-life - 10 days.
- Forcing fluids to tolerance (3-4 L/d) will reduce the biological half-life to 1/3 to 1/2 of the normal value.

NCRP 65 (1980) Rule of Thumb

- 1 µCi/L of urine equates to 10 mrem whole body dose (conservative)
- Five teens steal a H-3 exit sign and open it in an enclosed basement bedroom.
- Highest urine activity is approximately 5.8 µCi/L.
- Maximum estimate of CEDE is 58 mrem.
- This is a conservative estimate.

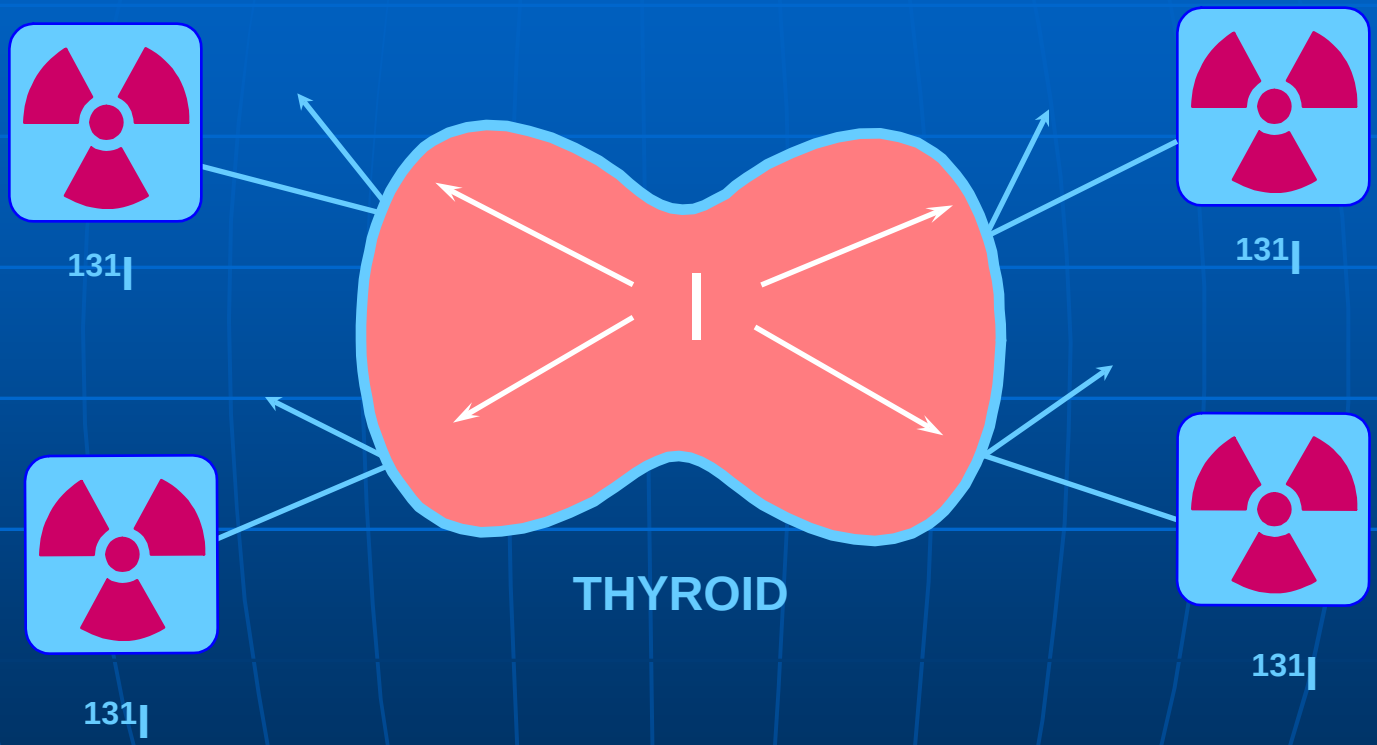
Strontium (Sr-90)

- Strontium-90 (Sr-90) is a by-product of the nuclear fission process, as found in nuclear power reactors or nuclear weapons. Sr-90 could be used by terrorists to create a radiological dispersal device (RDD or “dirty bomb”). It could also be released as the result of a catastrophic event at a nuclear power plant.
- Medical countermeasures include aluminum phosphate, aluminum hydroxide, barium sulfate, IV calcium gluconate, sodium alginate.

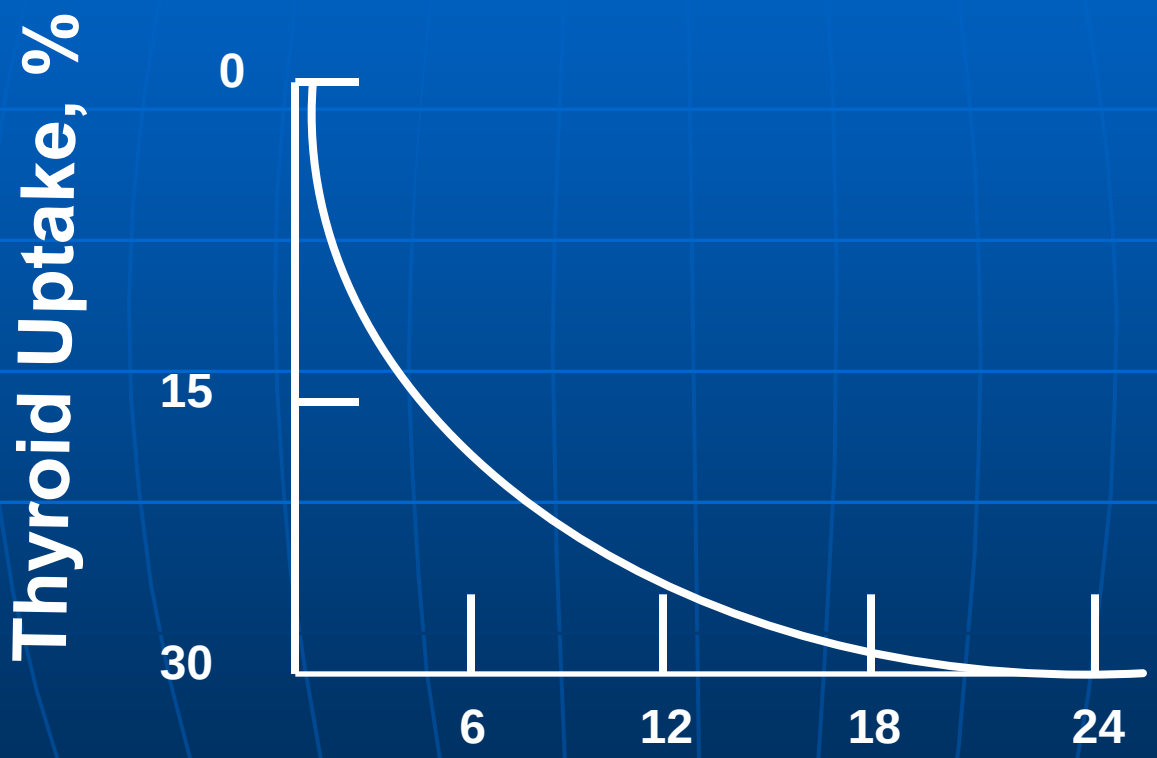
Iodine

- The dominant initial internal contaminant after a reactor accident, nuclear weapons test, or any incident involving *fresh* fission products is likely to be ^{131}I.
- Thyroid is generally blocked by dilution; 130 mg KI tablet stat and one tablet daily x 7-14 days.
- 5 or 6 drops of SSKI, Saturated Solution of Potassium Iodide (1 g/ml) is another convenient way to administer stable iodide.
- Potassium perchlorate (200 mg) may be used in patients with iodine sensitivity.

Saturate the Critical Organ with the Stable Isotope



Prompt KI Treatment of ^{131}I Intake is Highly Effective



FDA Recommendations for Potassium Iodide

- A daily dose of:
  - 16 mg of KI for infants <1 month
  - 32 mg of KI for children 1 month to 3 years
  - 65 mg of KI for children and teenagers 3 years to 18 years
  - 130 mg of KI for adults including pregnant and lactating women and adolescents over 150 pounds
- Daily dosing should continue until the risk of exposure has passed and/or until other measures (evacuation, sheltering, control of the food and milk supply) have been successfully implemented

Childhood Thyroid Cancer near Chernobyl

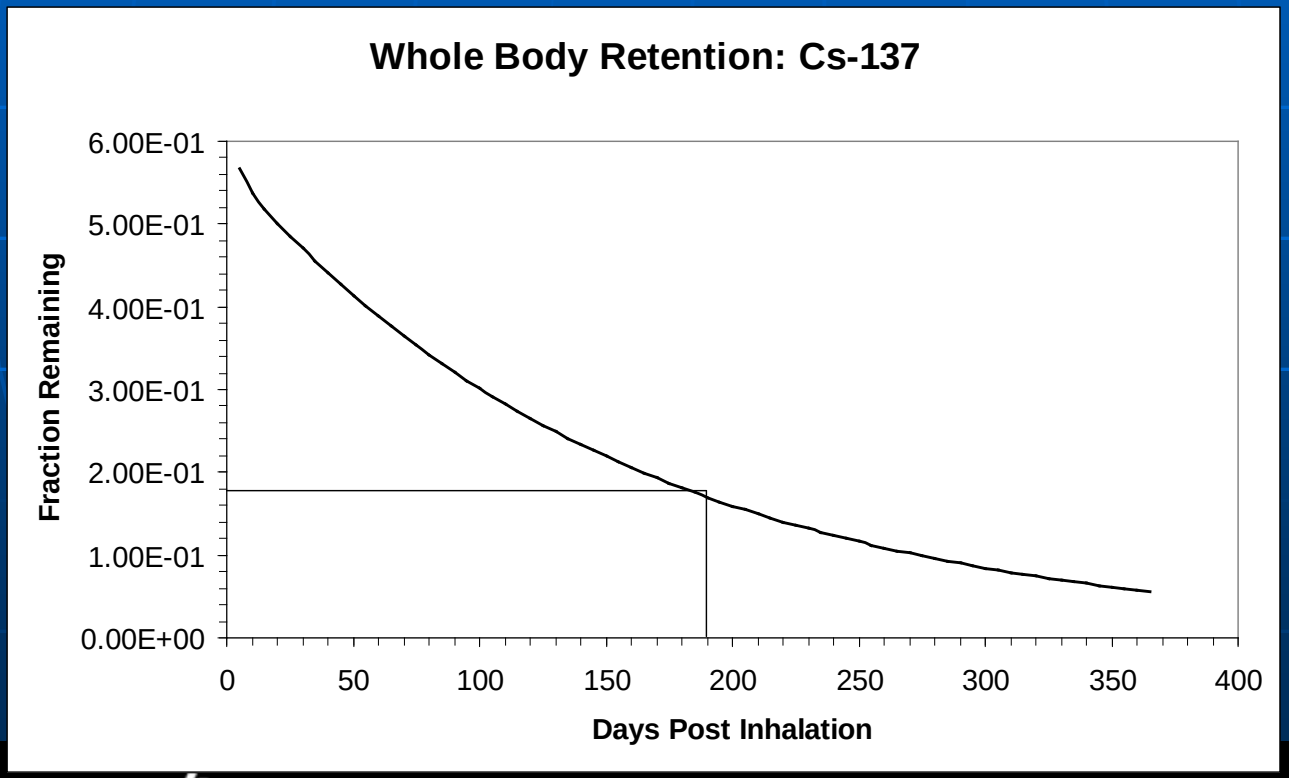
- In Gomel region of Belarus, north of Chernobyl, children were screened for thyroid cancer by physical examination, ultrasound imaging of the thyroid, and by thyroid function tests.
- Prior to the accident, thyroid cancer rate = 0.5/million. In the period 1991-1994, rate = 96.4/million. This represents almost a 200-fold increase.
- Reference: BMJ, vol 310, p 801, March 25, 1995.

Cesium

- ^{137}Cs (physical half-life, 30 years; biological half-life 109 days) is the dominant radioisotope in *aged* fission products.
- Distributes in body fluids similarly to potassium.
- The most effective means for removing radioactive cesium is the oral administration of ferric ferrocyanate, commonly called Prussian Blue.
- One gram orally three times daily x 3 weeks reduces the biological half-life to about 1/3 of the normal value. For higher intake, titrate upward.

Cs-137 Inhalation INTAKE: WHAT IS THE DOSE (CEDE)?

Step 1) Estimate the Intake Using Intake Retention Fractions.



At 190 days about 18% of Cs-137 Remains in whole body.

Example:Assume Lung Counts Measured 1.48 MBq [40 uCi] of Cs-137 at 190 Days

Intake (Inhalation) = 1.48 MBq/0.18 = 8.2 MBq

[40 uCi/0.18 = 222 uCi]

Step 2) Compare to Annual Limit on Intake (ALI).

ALI = 7.4 MBq [200 uCi] for Cs-137

(Gives 0.05 Sv [5 rem] CEDE)

So individual has 110% of ALI and

Dose of 0.55 Sv [5.5 rem]!

TREAT???

Prussian Blue is Highly Effective in Rx of Radio-Cesium or Thallium Uptake*

- Binds ions in gut
- Reduces biological half life to one third of untreated value
- Not absorbed
- Reduces recycling

*Complete package information available at www.orau.gov/reacts/resources.htm

Goiania Data

Table 2: Cesium-137 Effective Half-life During and After Treatment with Insoluble Prussian blue (In Days, by Age, and Dose of Insoluble Prussian blue)					
Group	**Age (Years)**	**Insoluble Prussian blue dose (grams/day)**	**No. of Pts.**	**During Insoluble Prussian blue Treatment - ^{137}Cs $T_{1/2}$**	**Off Insoluble Prussian blue Treatment - ^{137}Cs $T_{1/2}$**
Adults	> 18	10	5	26 ± 6 days	80 ± 15 days (all 21 adult patients)
Adults	> 18	6	10	25 ± 15 days	
Adults	> 18	3	6	25 ± 9 days	
Adolescents	12 -14	< 10	5	30 ± 12 days	62 ± 14 days
Children	4 - 9	< 3	7	24 ± 3 days	42 ± 4 days

Actinides

- Plutonium, Americium, Curium, and Californium.
- All have long biological half-lives.
- Inhalation is approximately 75% of industrial exposures.
- If the compound is soluble (nitrate, citrate, fluoride), compound is ultimately translocated from the lungs to ultimate disposition sites (bone and liver).
- Ca-DTPA and Zn-DTPA chelation therapy is the treatment of choice.

DTPA

- Trisodium calcium diethylenetriaminepentaacetate (Ca-DTPA).
- Chelating agent for transuranic elements.
- Ca-DTPA is approximately 10 times more effective than Zn-DTPA for initial chelation of transuranics. It is the treatment of choice for initial patient management. Must be given as soon as possible after accident.
- After 24 hours, Ca-DTPA and Zn-DTPA are essentially equally effective.
- Repeated dosing of Ca-DTPA can deplete the body of zinc and manganese.

DPTA Ampules
(1 gm per vial)

DTPA Dosing Schedules

- Dosage of Ca-DTPA and Zn-DTPA is 1 gm IV or inhalation in a nebulizer (1:1 dilution with water or saline).
- Very safe drug with no significant adverse reactions noted during 25 years of usage.
- Initially: 1 gm Ca-DTPA; repeat 1 gm Zn-DTPA daily up to five days if bioassay results indicate need for additional chelation.
- Ca-DTPA - Pregnancy category D; Zn-DTPA - Pregnancy category C.
- DTPA + DFOA may be a better combination.

NCRP 161 Writing Committee

William J Bair, PhD, Chairman

Wesley E Bolch, PhD (Univ. of Florida)

William E Dickerson, MD (Retired, AFFRI)

Keith F Eckerman ,PhD (ORNL)

Ronald E Goans, MD, PhD (MJW Corp.)

P Andrew Karam, PhD (NYC Health Dept.

Richard W Leggett, PhD(ORNL)

Joyce L Lipsztein, PhD(Univ. of Rio de Janeiro)

Michael G Stabin,PhD (Vanderbilt Univ.)

Albert L Wiley Jr. , BNE, MD, PhD(REAC/TS/NNSA)

NCRP Report No. 161: Management of Persons Contaminated with Radionuclides: Handbook

http://www.ncrponline.org/Publications/161press.html

William J Bair, *Chairman*
Pacific Northwest National Laboratory (retired)
Richland, Washington

Wesley E. Bolch
University of Florida
Gainesville, Florida

William E. Dickerson
Armed Forces Radiobiology
Research Institute
Bethesda, Maryland

Keith F. Eckerman
Oak Ridge National Laboratory
Oak Ridge, Tennessee

Ronald E. Goans
MJW Corporation
Clinton, Tennessee

P. Andrew Karam
New York City Department of
Health and Mental Hygiene
New York, New York

Richard W. Leggett
Oak Ridge National Laboratory
Oak Ridge, Tennessee

Joyce L. Lipsztein
State University of Rio de Janeiro
Rio de Janeiro, Brazil

Michael G. Stabin
Vanderbilt University
Nashville, Tennessee

Albert L. Wiley, Jr.
Radiation Emergency Assistance
Center/Training Site
Oak Ridge, Tennessee

NCRP 161 consists of
Volume 1 and Volume 2

Clinical Decision Guidelines (CDG)

- CDG = the maximum, once-in-a-lifetime intake of a radionuclide that represents:
  - ✓ "Stochastic risk, as judged by the calculated ED over 50Y for intake by adults and to age 70Y for intake by children, that is in the range of risks associated with guidance on dose limits for emergency situations (DOE, 2008a; FEMA, 2008; ICRP, 1991a; NCRP, 1993; 2005a)"

Clinical Decision Guidelines (CDG)

- CDG = the maximum, once-in-a-lifetime intake of a radionuclide that represents:
  - ✓ "Avoidance of deterministic effects as judged by the calculated 30d RBE-weighted absorbed doses to red marrow and lungs, with allowance for the significant uncertainties often involved in an initial evaluation of the chemical and physical form of a radionuclide and the level of activity taken into the body during an incident."

$$CDG = MIN\left[\frac{0.25\ \text{Sv}}{e(\text{Sv Bq}^{-1})}, \frac{0.25\ \text{Gy-Eq}}{d_{\text{Red Marrow}}(\text{Gy-Eq Bq}^{-1})}, \frac{1.0}{d_{\text{Lung}}(\text{Gy-Eq Bq}^{-1})}\right] \quad (11.1)$$

where:

e = effective dose coefficient for the radionuclide

$d_{\text{Red Marrow}}$ and d_{Lung} = RBE-weighted absorbed-dose coefficients for red marrow and lung, respectively

MIN = minimum value of the three arguments

NCRP 161: Decorporation Therapies

Radionuclide	Possible	Preferred
Actinium	Consider DTPA	Consider DTPA
Americium	DTPA	DTPA
Antimony	BAL, penicillamine	BAL
Barium	Ba, Ca therapy (Section 12.4.1.)	Same
Berkelium	DTPA	DTPA
Bismuth	BAL, penicillamine, **DMSA**	**DMSA**
Cadmium	**DMSA**, DTPA, EDTA	**DMSA**
Californium	DTPA	DTPA
Calcium	Ba, Ca therapy (Section 12.4.1)	Section 12.4.1.
Carbon	Consider hydration & non-rad C	Same
Cerium	DTPA	DTPA

* Not specifically discussed in NCRP Report # 65

161: Decorporation Therapies

Radionuclide	Possible	Preferred
Cesium	Prussian Blue	Prussian Blue
Chromium	DTPA, EDTA, no antacids	DTPA
Cobalt	**DMSA**, DTPA, EDTA, **NAC**	**DMSA**
Copper	**EDTA,** penicillamine**, trientine**	Pencillamine
Curium	DTPA	DTPA
Einsteinium	DTPA	DTPA
Europium	DTPA	DTPA
Mixed fission products	Depends upon predominant radionuclides: early – I; late: Sr, Cs	
Fluorine	Aluminum hydroxide	AlOH
Gallium	Consider penicillamine	Penicillamine
Gold	BAL, penicillamine	Penicillamine

161: Decorporation Therapies

Radionuclide	Possible	Preferred
Indium	DTPA	DTPA
Iodine	KI, consider SSKI, propylthiouracil, methimazole or potassiumiodate	KI
Iridium	Consider DTPA, EDTA	Consider DTPA
Iron	Deferoxamine (DFOA), deferasirox, DTPA, or DOFA + DTPA	DFOA
Lanthanum	DTPA	DTPA
Lead	**DMSA**, EDTA, EDTA + BAL	**DMSA**
Manganese	DFOA, DTPA, EDTA	DTPA
Magnesium	Consider Sr (Section 12.4.5)	Section 12.4.5.
Mercury	BAL; EDTA; penicillamine; DMSA	BAL
Molybdenum	Limited clinical experience	

161: Decorporation Therapies

Radionuclide	Possible	Preferred
Neptunium	Consider DFOA &/or DTPA	← Same
Nickel	BAL, EDTA	BAL
Niobium	DTPA	DTPA
Palladium	Penicillamine, DTPA	Penicillamine
Phosphorus	Phosphorus therapy	← Same
Plutonium	DTPA, DFOA, EDTA, DTPA + DFOA	DTPA
Polonium	BAL, DMSA, penicillamine	BAL
Potassium	Diuretics	Diuretics
Promethium	DTPA	DTPA
Radium	$AlP0_4$ gel, $BaSO_4$	← Same
Rubidium	Prussian Blue	Prussian Blue

161: Decorporation Therapies

Radionuclide	Possible	Preferred
Ruthenium	DTPA, EDTA	DTPA
Scandium	DTPA	DTPA
Silver	No specific therapy	
Sodium	Diuretics & isotopic dilution with 0.9% NaCl	← Same
Strontium	Multiple therapies (Section 12.4.5)	← Same
Sulfur	Consider sodium thiosulfate	← Same
Technetium	Potassium percholorate	← Same
Thallium	Prussian Blue	Prussian Blue
Thorium	Consider DTPA	Consider DTPA
Uranium	Sodium bicarbonate to alkalinize urine; consider dialysis	Bicarbonate

Case Study - Actinide Intake

- REAC/TS received an early AM call for assistance involving Pu 238.
- Laboratory medical personnel reported that a loss of containment incident involving 238Pu had occurred the previous evening and that four workers had had positive nasal smears (1250 dpm – 170,000 dpm alpha), indicating a high probability of inhalation.
- All four employees received an initial dose of Ca-DTPA the evening of March 16, 2000.

Case Study - Actinide Intake

- As part of the long-term medical management of this incident, a total of 99 doses of DTPA were given to these four individuals over 3 months.
- No adverse reactions were noted. In the first two months post-accident, urine excretion of Pu-238 was approximately linear with time, indicating a medically significant response to the DTPA therapy.
- According to the DOE DTPA Registry maintained by REAC/TS, this incident to date has resulted in the third highest number of DTPA doses given for a single case. All four patients have continued to do well post-chelation therapy

Case History: Pu-239 in finger wound

- Industrial accident in 1991 involving deep, contaminated wound (Pu-239/Am-241 oxide) to left thumb.
- DTPA given at the time of incident and subsequently.
- Multiple wound and whole body counts using high resolution Ge detectors and Phoswhich detectors.
- Translocation of Pu-239 from wound to liver and bone. Effective half-life from wound was approximately 1500 days.

Death By Internal Contamination (Po 210)

- 1 Nov 2006 – Litvinenko meetings in a London hotel and sushi bar. Hour later complains of feeling sick, vomiting
- 4 Nov – admitted to Barnet General Hospital in north London
- 17 Nov – transferred to University College Hospital - placed under armed guard
- 19 Nov – report: Litvinenko poisoned by thallium
- 21 Nov – suggestion - radioactive thallium?
- 22 Nov – thallium ruled out

Death from Po2109(cont)

- 23 Nov 2006 – Litvinenko dies
- 24 Nov – suspect radiation related death - traces of radioactive material found in sushi bar and hotel
- 26 Nov – calls start to the NHS, by 11/28 over 1100 people have called and 65+ have been assessed
- 29 Nov – traces of Po-210 found on airliners
- 4 Dec – so far: 3000+ calls to NHS, 179 follow-ups, 27 referrals, 70 urine samples (negative)
- 6 Nov – declared a murder by British police

Death from Po210(cont.)

- 3 Jan 2007 – 12 people reported "affected by the radioactive substance" to date

- 11 Jan – to date:
  - 120 of 596 people tested for Po-210 showed "traces of radiation"
  - 13 deemed to have some stochastic health risks, but long-term risk is small
  - 450 people identified world-wide as "affected by radiation" – working with 48 different countries

Issues/Considerations

- Population Monitoring
  - Alpha monitoring capabilities are required (gamma yield 1.06E-5)
  - Polonium bioassay methodology
  - Data interpretation

- Medical Management
  - Chelation – few studies in humans; ?BAL (NCRP 161)

- Public Health Issues (general public and health care workers)
- HPA found that the usual PPE for health care workers was quite sufficient since workers had much less exposure than some members of the public.

Internal Contamination Summary

- Intakes of radionuclides can be treated successfully
- The appropriate treatment is element-specific, so the contaminant must be identified
- The sooner treatment is begun, the better
- Key Reference: NCRP 161, Management of Persons Accidentally Contaminated with Radionuclides

- Thank you!
- Questions?

- Acknowledgements:
- Some of the slides in this presentation were from presentations given at REAC/TS lectures by Tom McVitte ,PhD(AFRRI and Univ. of Maryland),R.Toohey,PhD(ORAU) and Dennis Confer,MD(National Bone Marrow Program and Univ. of Minn.)

- albert.wiley@orise.orau.gov